

REMARKS

Claims 1-18 and 22 are pending, and claims 1-18 and 22 stand rejected.

Claim Rejections Under 35 USC § 103

Claims 1-17 and 22 stand rejected under 35 U.S.C. §103(a) as being unpatentable over U.S. Patent 7,065,236 to Marcellpoil et al. ("the '236 patent") in view of U.S. Patent 4,090,243 to Kotera et al. ("the '243 patent").

The rejection of claims 1-17 and 22 is respectfully traversed. The Examiner asserted that the '236 patent (Marcellpoil) discloses measuring a color channel value in a plurality of pixels from a control sample comprising a single color of interest (col. 8/14-23: camera 300 captures a color image of a sample 500 - the image having red, green, and blue color channel values). However, the '236 patent does not disclose a control sample comprising a single color of interest, and in fact does not disclose a *control* sample at all. The prepared sample (500) is measured by the system 100 for, for example, thickness and optical density. (Col. 11, line 63 - col. 12, line 35). The '236 patent does not disclose a control sample which is the basis for a vector which comprises an average of each color channel value present in the control.

The Examiner asserted that the vector for the control sample is defined by the optical density vector OD, given by equations 3-5 or 6-8 in column 11, the vector comprising the measured optical densities for the red, green, and blue color channels. However, the '236 patent does not disclose a control sample, hence the '236 patent cannot disclose a vector for the control sample. The '236 patent, at col. 11 noted by the Examiner, does not disclose a control sample for each dye that would be the basis for a vector of the average r, average g, and average b values. The equations 3-5 or 6-8 define the optical density in the red, green and blue channels

for x number of dyes in a prepared sample (e.g., a marker dye for targeting the molecular species of interest and a counterstain for staining the remainder of the sample). (Col. 9, lines 12-16; col. 10, line 63-col. 11, line 7). Further, in the rejection of claims 4 and 13 (page 8) the Examiner refers to the sample of Col. 10/63 et seq. as an experimental sample. The Lambert-Beer law, upon which the '236 patent is based, is additive so that the optical density for the prepared sample in, for example, the red color channel, is the sum of the optical densities of all of the dyes in the prepared experimental sample, measured in the red color channel. This is distinct as compared to developing a vector of the average r, average g, and average b values of all pixels of *a control sample of one color/stain*, and developing such a vector for *each* control sample.

Further, it is these vectors of the average r, average g, and average b values, for each control (each control consisting of one color or stain), that combine to build the matrix and, thus, the conversion matrix. The matrix of the '236 patent is based upon optical densities and relative absorption coefficients of dyes of the sample, as there is no control sample. (Col. 14, lines 7-52; col. 15, lines 63-67). The process of the '236 patent is also dependent upon the use of a particular light source (similar spectral characteristics) and the transmitted light intensity. The relative absorption coefficients are used to determine the relative concentrations of the dyes. (col. 16, lines 9-40). The process of the '236 patent is dependent upon the Lambert-Beer law. This process is distinct as compared to the process of the instant application.

The Examiner asserted that the '236 patent seems to utilize a single control sample, however the '236 patent does not identify a control sample and does not characterize this control sample. The Examiner has not identified the control sample of the '236 patent; the sample 500, as noted above, is a prepared sample, a sample requiring identification of the concentrations of

dyes via relative optical densities and relative absorption coefficients. (Col. 13, lines 25-31). For at least the reasons articulated above, the '236 patent does not disclose all of the elements of independent claims 1 or 10.

Further, both independent claim 1 and independent claim 10 recite defining "a vector for each of the plurality of control samples, wherein each vector comprises an *average of each color channel value* present in the control" and defining "a matrix comprising *each of the averages for each of the color channels*." Neither the '236 patent or the '243 patent discloses obtaining an average of each color channel value. The '236 patent generally discusses obtaining the absorption coefficients for a dye in the red, green and blue channels and obtaining optical densities measured in the red, green and blue channels, but not, as noted by the Examiner, taking the *average* of a color channel value. (Col. 11, lines 4-19). Further, the '243 patent does not disclose a vector comprising color channel value measurements; color channel measurements are not disclosed in the '243 patent. Hence, the combination of the '236 patent and the '243 patent do not disclose each and every element of independent claim 1 or 10.

The Examiner further asserted that Kotera ("the '243 patent") "discloses a system...for characterizing the colors of a color sample that is very similar to that of Marcellpoil [that of the '236 patent,] and involves the same concepts of deriving an inverse matrix of mean color intensity values...and using the inverse matrix to ascertain the colors of an experimental sample." (Col. 5, lines 1-35; 58-66). However, the '236 patent, as noted above, does not disclose a similar system to that of the '243 patent. The '236 patent does not involve the concept of deriving an inverse matrix of mean color intensity values. The '236 patent involves deriving an inverse matrix of absorption coefficients, and no mean values of any kind are calculated. (Col.

14, lines 43-55). The '243 patent is directed to identification of a color in a painted print by using Bayes' Rule, where the product  $P(C_i)p(x|C_i)$  equals the joint probability density  $p(x, C_i)$  which is the probability of simultaneous occurrence of "x" and " $C_i$ "; the probability of color  $C_i$  occurring at position x. A control sample of the color is provided and mean values  $\mu^{(i)}$  are derived from the color sample. The '243 invention is based upon the notion that colors of a print can be identified with the highest degree of certainty by two probabilities; the probability of occurrence of each color as the print is scanned across its surface, and the probability that an observed color spectral component corresponds to a particular color sample. Hence, the '243 patent is directed to *recognizing colors* with a high degree of certainty. The '243 patent is *not* directed to determining how much or the concentration of a color or dye, but the mere presence of a color. The '243 patent does not discuss use of coefficients of absorption, of optical densities, or of the Lambert-Beer law. Hence, the underpinning of the methodology of the '243 patent is distinct as compared to the '236 patent; the systems are not similar. Because the systems are not similar, there is little motivation to look to a system for determining *presence of a color* (and the color is previously identified) without use of impermissible hindsight.

The Examiner then asserted that it would have been obvious to modify the '236 patent by the '243 patent to achieve the instant invention by measuring a plurality of control samples and defining the vector and the matrix on the basis of an average of each color channel (e.g. r, g, b) present in the control samples. However, the '243 patent does not disclose defining the vector and the matrix on the basis of an average of each color channel present in the control samples. The '243 patent does not take an average of each color channel, but of a color sample. Further, the '243 patent derives a conversion matrix for the purpose of defining a probability that a

particular color is present in a particular location. The '243 patent does not address the *concentration or amount* of the color. Utilizing the teachings of the '243 patent leads to the probability/determination of the *presence of a particular color* or species at a particular location. On at least this basis, the teachings of the '243 patent and the '236 patent are not susceptible to combination.

The '236 patent tends to teach away from the notion of measuring control samples. As noted in the '236 patent, the Lambert-Beer law generally describes a proportionality that can be observed between the concentration of molecules in a solution (concentration of the molecular specie or the sample) and the light intensity measured through the solution. The Lambert-Beer law is typically expressed as  $OD = \epsilon \cdot l \cdot C$ , where OD is the optical density of the solution,  $\epsilon$  is a proportionality constant called the molar extinction or absorption coefficient,  $l$  is the thickness of the sample, and  $C$  is the concentration of the molecular specie. The absorption coefficient  $\epsilon$  is specific to the molecular specie. (Col. 8, lines 30-44). As noted at col. 13, lines 10-62, the absorption coefficient  $\epsilon$  of a dye can be determined once the optical density is known (OD) and if  $l \cdot C$  are known, but  $l \cdot C$  are typically not known for a particular pixel in an image of a particular sample, therefore the absorption coefficients are computed for each channel according to the ratio of the optical density in each channel, measured at a given pixel, to the maximum optical density out of all the channels measured at the same pixel. Once the optical densities have been determined from image data, and the absorption coefficients  $\epsilon$  have been evaluated for the different dyes, the equations can be solved for the respective concentrations of the dyes (e.g.  $C_1$ ,  $C_2$ ,  $C_3$ , etc.) Hence, the process of the '236 patent is relative and works within its own data set, and is not susceptible to combination with the '243 patent.

The Examiner asserted that the '236 patent and the '243 patent are related to the broad field of image analysis, and to the narrow problem of determining the constituent colors contained in a sample under examination, in accordance with the claimed invention of "quantifying a color in a sample." The Examiner asserted that both the '236 patent and the '243 patent are directed to determining colors present in samples. However, the '243 patent is related to a color separating system and a method and apparatus for separating colors of an original print painted with a number of predetermined colors and using probability and statistical data handling techniques for eliminating errors arising from the ambiguous color spectral information. (Col. 1, lines 5-13). The '243 patent is directed to using these probability and statistical data handling techniques to determine the *presence* of a color at a particular location, the color having been previously identified. The '236 patent is directed to determining the concentration, the amount present of a molecular specie as indicated by the respective dye. The problem to be solved by the '243 patent is distinct as compared to the '236 patent and the instant application, and is not susceptible to combination with the '236 patent. The field of image analysis is an overly-broad identifier.

An inventor would not have been reasonably motivated to consult references describing determining the presence of a color through use of probability and statistical data handling (e.g. to recreate a color print painted by artisans) to solve the problem of determining the concentration or amount of a particular dye. "The combination of elements from non-analogous sources, in a manner that reconstructs the applicant's invention only with the benefit of hindsight, is insufficient to present a *prima facie* case of obviousness." *In re Oetiker*, 977 F.2d 1443, 24 USPQ2d 1443. The Examiner states that the '243 patent is relied on only for the

narrow teaching that it was conventional to utilize a plurality of control samples in a process for identifying the color of experimental samples. The identification of the presence of an already identified color is inapposite to the nature of the '236 patent and the instant application. The combination of the '236 patent and the '243 patent is made with the impermissible use of hindsight.

The Examiner asserted that the stringent requirements of the teaching-suggestion-motivation (TSM) test and established motivation or suggestion does not necessarily need to be present for a claim to be rendered obvious. But, it is still required that the prior art reference (or references, when combined) must teach or suggest all the claim limitations. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991). MPEP §2142. As noted above, the combination of the '236 patent and the '243 patent do not teach or suggest all the claim limitations.

For at least the above-noted reasons, independent claims 1 and 10 allowable and are not obvious. Claims 2-9, 11-17, and 22 depend from claims 1 and 10, respectively, and are also allowable and not obvious. Reconsideration and withdrawal of the rejection of claims 1-17 and 22 are respectfully requested.

#### Rejection of Claim 18

Claim 18 is rejected under 35 U.S.C. §103(a) as being unpatentable over U.S. Patent 7,065,236 to Marcelpoil et al. ("Marcelpoil") in view of U.S. Patent 4,090,243 to Kotera et al. ("Kotera") and U.S. Patent Application Publication 2004101 14227 by Henderson et al. ("Henderson").

The Examiner asserted that Marcelpoil discloses a machine vision system (figures 1 and 2) for automated analysis of a biological sample on a slide. This rejection is respectfully traversed.

The cited references of Marcelpoil, Kotera and Henderson do not teach or suggest all the claim limitations of independent claim 18. Independent claim 18 recites defining “a vector for each of the plurality of control samples, wherein each vector comprises an *average of each color channel value* present in the control” and defining “a matrix comprising *each of the averages for each of the color channels*.” Neither the ‘236 patent or the ‘243 patent discloses obtaining an average of each color channel value. The ‘236 patent generally discusses obtaining the absorption coefficients for a dye in the red, green and blue channels and obtaining optical densities measured in the red, green and blue channels, but not, as noted by the Examiner, taking the *average* of a color channel value. (Col. 11, lines 4-19). Further, the ‘243 patent does not disclose a vector comprising color channel value measurements; color channel measurements are not disclosed in the ‘243 patent. Hence, the combination of the ‘236 patent and the ‘243 patent do not disclose each and every element of independent claim 18. The addition of Henderson does not make-up for the deficiency in the combination of the ‘236 patent and the ‘243 patent.

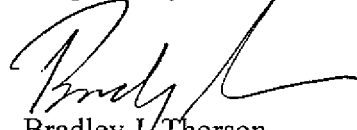
As noted in the discussion of independent claims 1 and 10 above, the ‘236 patent does not disclose a control sample for each dye that would be the basis for a vector of the average r, average g, and average b channel values. The arguments presented above in the discussion of independent claims 1 and 10 are repeated herein by reference, with respect to independent claim 18, as independent claim 18 contains the method of claim 1 and the instructions of claim 10 (except for outputting the amount of color in the experimental sample). Henderson is cited for



disclosing an automated slide loader for use with a microscope. However, Henderson does make-up for the deficiencies of the combination of the '236 patent and the '243 patent. Therefore, the combination of the '236 patent, the '243 patent and Henderson still does not disclose all the elements of claim 18. Thus, claim 18 is non-obvious over the '236 patent in view of the '243 patent and Henderson. For at least the above reasons, independent claim 18 is allowable and non-obvious. Reconsideration and withdrawal of the rejection of claim 18 are respectfully requested.

The Examiner is invited to telephone the undersigned if the Examiner believes it would be useful to advance prosecution.

Respectfully submitted,



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